

REMARKS

Applicants respectfully request that the Amendment filed on March 10, 2003 not be entered into the record, but replaced by the this amendment. Applicants are separately submitting a Peition and Fee For Extension of Time Under 37 C.F.R. § 1.136(a).

I. Drawings

Applicants note requested drawing changes. Applicants submitted separately to draftsperson on January 15, 2003, acceptable corrected drawings.

II. Claim Objections

Claims 6, 7, 9, 20, 22, and 23 were objected to because of the following informalities: In line 1 of claims 6, 7, 22, and 23, "A" should be --The--. Appropriate correction is required.

Applicants have amended claim 6, 7, 9, 22, and 23 by replacing a with --The--, thus alleviating this rejection.

In claims 19 and 20, line 3, the Examiner states the article "a" should be --the--.

Applicants have amended claims 19 and 20 by replacing "a" with --the--, thus alleviating this rejection.

III. Claim Rejections—35 U.S.C. § 112

Claims 1-10 and 18-35 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In claims 1, 5, and 8, the recitation "making available to the plant a transposase" in lines 3-4 of claim 1, line 6 claim 5, and lines 6-7 of claim 8 render them indefinite. The Examiner states that it is not exactly clear what is meant by making something "available" to a plant, especially since the recombination event of the claimed method is occurring within the cells of

the plant. It is suggested that the recitation be replaced with -- expressing a transposase within the plant --.

Applicants have amended claims 1, 5, and 8 by replacing "making available to the plant a transposase" with --introducing a transposase to the plant--, thus alleviating this rejection.

In the claim 5, the recitation of "a functional gene" in line 7-8 renders the claim indefinite. The Examiner states that it is not clear if the gene of the recitation is referring to the same functional gene mentioned in line 5 or a different one. It is suggested that the article "a" in line 7 be replaced with --said--.

Claim 5 has been amended by replacing "a" with --said-- in line 7 as suggested by the Examiner, thus alleviating this rejection.

In claim 6, 9, 25, 33, and 35, the recitation "commercially enhancing a biosynthetic pathway" renders the claim indefinite. The Examiner states it is not clear what is meant by the recitation. The metes and bounds of the claim are not clear.

Applicants have amended these claims by deleting the recitation "commercially enhancing a biosynthetic pathway" and replacing it with specific commercially enhancing biosynthetic pathways, thus alleviating this rejection. Support is found on page 10, lines 7-8 of the specification.

In claim 8, the claim recites the recitation the limitation "the transposase" in lines 6-7. The Examiner states there is insufficient antecedent basis for this limitation in the claim.

Claim 8 has been amended in response to another rejection. It is believed that proper antecedent basis is recited in the amended claim, thus alleviating this rejection.

The Examiner further states that in claim 8, the claim is written in a confusing manner. Lines 1-5 indicate that the transcription/translation of a gene will occur when the overlapping

sequences have recombined to result in a gene. However, line 5 indicates that the transposase is made available "subsequently", after the recombination event. The Examiner states that this is confusing since the transposase is required for the recombination event. The recitation "a method to induce transcription and/or translation of a gene" in line 1 also renders the claim indefinite. The promoter would have been recognized by RNA polymerase regardless of the recombination event. The recombination event itself does not have anything to do with the induction of transcription or translation. It is also inaccurate to state that a gene is translated. The recitation "a maize Ds element containing overlapping sequences having homologous regions" in lines 2-4 of claim 8 also renders the claim indefinite. The specification of Figure 1 indicates that the overlapping homologous regions are shared by the fragments of a gene that are combined by the recombination event. The gene fragments are not internal to the Ds element, but rather flank it.

Applicants have amended claim 8 to more clearly state that the transposase can be introduced with the recombination construct, or subsequent to the transformation of the recombination construct. Support is found in the specification on page 8, lines 20-24. Applicants respectfully bring to the attention of the Examiner that the recombination construct of claim 8 comprises a Ds element flanked by overlapping sequences having homologous regions when recombined. This language indicates that upon recombination, these homologous regions exist, not that recombination has taken place. Additionally, Applicants have amended claim 8 to recite "a method to induce recombination", in line 1. Applicants respectfully submit that the recitation "a maize Ds element containing overlapping sequences having homologous regions" in lines 2-4 claim 8 is not indefinite. Applicants define on page 7 that the phrase "overlapping sequences having homologous regions" means the entire sequence that encodes the construct

desired must be represented by two fragments and that some of the same internal sequences must exist on each of the two fragments so as to allow recombination of the fragments to produce the complete construct. It is black letter law that the patentee can "choose to be his or her own lexicographer by clearly setting forth an explicit definition for a claim term with a different scope from that which would be afforded by its ordinary meaning." Rexnord Corp. v. Laitran Corp., 274 F.3d 1336, 1342, 60 U.S.P.Q.2d 1851, 1854 (Fed. Cir. 2001). "The specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582, 39 U.S.P.Q.2d 1573, 1577 (Fed. Cir. 1996). Here, the Applicant has clearly defined a claim term in which the definition is the best guide to the meaning of this particular term. Therefore, Applicants respectfully submit that claim 8 is now in allowable form. Applicants respectfully request the Examiner to withdraw this rejection.

In claim 18, the recitation "introduction of a maize transposase" in line 2 renders the claim indefinite. The Examiner states it is not clear if the maize transposase is being inserted into the construct. If it is not, it is not clear what the transposase is being introduced into. It is suggested that the recitation "upon introduction" be replaced with --in the presence--. Further, it is suggested that the recitation --, said construct-- be inserted in line 2 before "comprising", so that the claim unambiguously indicates that the repeat sequences are within the construct.

Applicants have amended claim 18 as suggested by the Examiner, thus alleviating this rejection.

In claims 19 and 20, the recitation "a maize transposase comprising a maize recombination construct" in lines 2-4 renders the claim indefinite. The Examiner states the recitation appears to indicate that the transposase comprises a nucleic acid construct. It is

suggested that the recitation --, said composition of matter -- be inserted into line 3 after "transposase."

Applicants have amended claims 19 and 20 according to Examiner's suggestion, thus alleviating this rejection.

In claim 20, the recitation "a maize recombination construct of claim 18 in a plant" renders the claim indefinite. The Examiner states it is not clear what this recitation is referring to.

Applicants have amended claim 20 by deleting the recitation " a maize recombination construct of claim 18 in a plant" and replacing it with --direct repeat sequences proximal to a Ds element and an agronomically significant gene internal to the direct repeats in a plant transformed with said construct-- to make it more clear what this recitation is referring to.

In claims 19, 20, 22, and 23, the recitation "composition of matter", renders the claims indefinite. The Examiner states DNA molecules can be induced to undergo homologous recombination. However, it is not clear what else is encompassed by the recitation, as the claims indicate that it is the composition of matter that undergoes recombination. The metes and bounds of the claims are not clear. The claims also broaden the scope of parent claim 18, which is directed to a recombination construct. Claims 19, 20, 22, and 23, however, are drawn to any composition of matter.

Applicants have amended claims 19, 20, 22, and 23 by deleting the recitation "a maize recombination construct of claim 18" and inserting -- direct repeat sequences proximal to a Ds element and an agronomically significant gene internal to the direct repeats-- to more clearly show what is encompassed by the recitation "composition of matter", thus alleviating this rejection.

IV. Claim Rejections—35 U.S.C. § 102

Claims 1-4, 27, 28, and 32 were rejected under 35 U.S.C. § 102(b) as being anticipated by Shalev et al. The Examiner states Shalev teaches an assay for homologous recombination induced by the maize Ac transposase in transgenic tobacco plants. The plants were transformed with constructs containing the maize Ds element flanked by direct repeats. Recombination induced by Ac resulted in the combination of GUS deletion mutants to yield an intact, functional GUS gene.

Although not acceding to the Examiner's rejection, Applicants are herein submitting for consideration by the Examiner the declaration of Dr. Yongli Xiao under 37 C.F.R. 1.131, to overcome the Shalev reference cited by the Examiner.

V. Claim Rejections—35 U.S.C. § 103

Claims 1-10 and 18-35 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Swoboda et al. in view of Shalev et al., Holtorf et al., Hain et al., and Fromm et al.

Applicants respectfully traverse this rejection. The cited references taken together fail to suggest the claimed invention. The Federal Circuit has held absent any disclosure or suggestion of a missing element, there can be no motivation to modify the prior art to arrive at the claimed invention. See *In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313 (Fed. Cir. 2000). Furthermore, it is impermissible to use the claims as a framework from which to pick and choose among individual references to recreate the claimed invention. *In re Fine*, 5 USPQ2d 1596, 1600 9 (Fed. Cir. 1988). As stated by the Examiner, Swoboda fails to teach homologous recombination induced by a transposase or an inducible promoter, disease resistant genes, or transgenic maize plants. Therefore, Swoboda does not teach these missing elements as claimed by the Applicants (See, for example claim number 26, which depends from claim 3, wherein

Applicants teach an inducible promoter. Thus, one of ordinary skill in the art would not be motivated to make the combination as suggested by the Examiner.

Moreover, for reasons previously stated, Shalev does not teach or suggest the elements of claims 1-10 and 18-35. Shalev teaches an assay where one recombination partner carries a deletion at the 5' end of the GUS gene and a Ds or Ac element inserted into the deletion site and the other recombination partner carries an intact 5' end of the GUS open reading frame and has a deletion at the 3' end of the gene. Shalev's assay finds that the excision of Ac induces recombination between nonallelic sequences. (See Figure 1B). On the contrary, Applicants' claimed invention teaches a method to induce homologous recombination in a plant containing a recombination construct and a source of Ac transposase. There is no excision of the Ac element from the claimed construct. Shalev fails to teach or suggest this.

Holtorf et al. merely teaches heat shock promoters. There is no teaching or suggestion that it be combined in the manner suggested by the Examiner. Absent such a suggestion, a person skilled in the art would have no motivation to include the Ac transposase coding sequence on the recombination construct and to place it under the control of an inducible promoter. Holtorf fails to teach introducing any recombination construct to the plant in expressing an Ac transposase to induce homologous recombination wherein the recombination construct further comprises a transposase gene under the control of an inducible promoter.

Hain et al. merely teaches enhanced disease resistance against fungal infection in transgenic tobacco plants conferred by a grape stilbene synthase gene. There is no teaching or suggestion in Hain to replace the sequences encoding the GUS gene fragments with fragments of any other gene of interest, i.e., the stilbene synthase gene as taught by Hain et al.

Fromm et al. merely teaches the production of transgenic maize plants. There is no suggestion or teaching, nor would one of ordinary skill in the art be motivated to make the combination stated by the Examiner. Fromm fails to teach that element limitations of claims 1-10; 18-35, introducing a recombination construct to the plant and expressing a transposase within the plant so as to induce homologous recombination, wherein the recombination construct comprises a maize Ds element, and wherein the recombination construct further comprises direct repeat proximal to the Ds element and wherein the recombination construct for the comprises a transposase gene under the control of an inducible promoter. Therefore, Applicant's claims are patentable over Swoboda in view of Shalev, Holtorf, Hain, and Fromm.

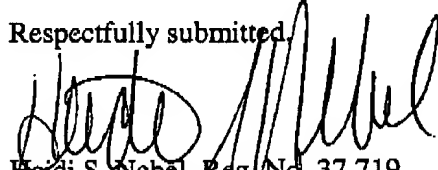
Additionally, a reference does not contain a suggestion to combine if it teaches away from the invention. *Tec Air, Inc. v. Denso Mfg. Michigan, Inc.*, 192 F.3d 1353, 1360 52 USPQ2d 1294 (Fed. Cir. 1999). A reference teaches away if one of ordinary skill in the art would be discouraged from following the path set out in the reference. *Id.* Shalev teaches away from the claimed method because Shalev teaches that GUS reactivation only occurs with Ac in 3' Δ GUS x 5' Δ GUS: Ac crosses, but not with the Ds element. (See column 1, page 1148). Conversely, Applicant's invention is directed to the finding that overlapping foreign gene sequences containing a maize Ds element can be induced to undergo homologous recombination upon introduction of the maize Ac transposase. The Ac transposase has been shown by the Applicants to induce recombination of the foreign GUS gene fragments to produce a functional GUS gene. Thus, Shalev teaches away because one of ordinary skill in the art would be discouraged from following the path set out in Shalev in order to arrive at Applicants' claimed invention.

VI. Conclusion

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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Application No. 09/696,600

**AMENDMENT — VERSION WITH MARKINGS
TO SHOW CHANGES MADE**

In the Specification

Please delete the paragraph below on page 4 under "BRIEF DESCRIPTION OF THE DRAWINGS":

Figure 1 is schematic of a GU-Ds-US construct.

Figure 2A[, upper panel,] is a map of a GU-Ds-US construct, showing primer construct location and[, lower panel,] Figure 2B is a agarose gel showing PCR amplification products for certain pairs of primers.

Please delete the paragraph below starting on page 7, starting at line 13:

By "overlapping sequences having homologous regions" or "overlapping sequences having homologous sequences" it is meant that the entire sequence which encodes the construct product (or regulatory region) desired must be represented by the two fragments, and that [the] some of the same internal sequences must exist on each of the two fragments so as to allow recombination of the fragments to produce a complete construct. The gene product need not be a naturally-occurring gene product, nor need encode an independently-functional gene product. It could, for example, encode a fusion protein or sub-unit of a functional complex. Additionally, it could encode [an] a complementary transcript useful for inhibiting translation of mRNA. Lastly, the sequences could be nonsense sequences used simply for their ability to recombine.

Please delete the following paragraph on page 21 starting at line 14 with the following:

Among the progeny of the variegated GUS+ plants, was detected several plants with uniform GUS+ expression. To test for germinal transmission of a recombined GUS transgene, the genomic DNA from plants with uniform GUS expression by Southern hybridization was analyzed. Hybridization with a GUS-specific probe detected two bands (7.3 kb and 4.7 kb) in HindIII-digested DNA from a plant of genotype GU-Ds-US/-, sAc/- [(Figure 4a, lane 2)], whereas the GUS-specific probe detected only one band of 5.0 kb in DNA from two plants with uniform GUS expression. These results are expected from the generation of a single GUS coding sequence by recombination between the homologous regions of the GU-Ds-US construct. To verify that the recombinant GUS+ plants were derived from the original GU-Ds-US transformants, additional Southern hybridizations were performed using enzymes that cleave in the DNA flanking the transgene insertion. Genomic DNA from plants of genotype GU-Ds-US, sAc and the uniform GUS+ plants were digested with EcoRV and hybridized with a probe specific for the 3' end of the GU-Ds-US construct (Figure 1). The probe hybridizes to the same 4.2 kb band in the GU-Ds-US progenitor plants and the uniform GUS+ plants. This result indicates that the two GUS+ plants could not have arisen by seed or pollen contamination, but did in fact originate by recombination of the GU-Ds-US transgene locus.

In the Claims

Please amend claims 1, 5-9, 18-20, 22-23, 25, 30, 33, and 35 as follows:

1. (Amended)

A method to induce homologous recombination in a plant, comprising introducing a recombination construct to the plant, and [making available to the plant a transposase] introducing a transposase to the plant, so as to induce homologous recombination.

5. (Amended)

A method to construct a functional gene in plants, comprising introducing to the plant a maize recombination construct having overlapping sequences having homologous regions, which sequences, when homologously recombined, result in a functional gene, and [making available to the plant a maize transposase] introducing a transposase to the plant, so as to induce recombination and construction of [a] said functional gene.

6. (Amended)

[A] The method of claim 5, wherein the functional gene is selected from the group consisting of: genes useful for disease resistance; genes useful for male sterility; genes useful for environmental condition tolerance; and genes useful for [commercially-enhancing a biosynthetic pathway] fruit ripening, oil or pigment biosynthesis, seed formation, and starch metabolism.

7. (Amended)

[A] The method of claim 5, wherein the plant in which recombination is induced is selected from the group consisting of: soybean; maize; sugar cane; beet; tobacco; wheat; barley; poppy; rape; sunflower; alfalfa; sorghum; rose; carnation; gerbera; carrot; tomato; lettuce; chicory; pepper; melon; Arabidopsis; and cabbage.

8. (Amended)

A method to induce [transcription and/or translation of a gene] recombination in a plant comprising introducing to the plant a maize Ds element containing overlapping sequences having homologous regions[, which sequences, when homologously recombined, result in a gene] to a fragment of a gene; and [subsequently making available] introducing subsequently to the transformation of said Ds element [to the plant the] a transposase, so as to induce homologous recombination and subsequent transcription [and translation] of said gene.

9. (Amended)

[A] The method of claim 8, wherein the gene is selected from the group consisting of [those genes useful for]: genes useful for disease resistance; genes useful for male sterility; genes useful for environmental condition tolerance; and genes useful for [commercially-enhancing a biosynthetic pathway] fruit ripening, oil or pigment biosynthesis, seed formation, and starch metabolism.

18. (Twice Amended)

A recombination construct which can be induced to undergo homologous recombination [upon introduction] in the presence of a maize transposase, said construct comprising direct repeat sequences proximal to a Ds element and an agronomically significant gene internal to the direct repeats.

19. (Amended)

A composition of matter which can be induced to undergo homologous recombination upon introduction of a maize transposase, said composition of matter comprising [a maize recombination construct of claim 18] direct repeat sequences proximal to a Ds element and an agronomically significant gene internal to the direct repeats as part of a vector.

20. (Amended)

A composition of matter which can be induced to undergo homologous recombination upon introduction of a maize transposase comprising [a maize recombination construct of claim 18] direct repeat sequences proximal to a Ds element and an agronomically significant gene internal to the direct repeats in a plant transformed with said construct.

22. (Amended)

[A] The composition of matter of claim 20, which further comprises a gene internal to said direct repeat sequences.

23. (Amended)

[A] The composition of matter of claim 20, wherein said direct repeat sequences are in the form of overlapping sequences having homologous regions.

25. (Amended)

The method of claim 24, wherein the agronomically significant gene is selected from the group consisting of: genes useful for disease resistance; genes useful for male sterility; genes useful for environmental condition tolerance; and genes useful for [the commercially-enhancing a biosynthetic pathway] fruit ripening, oil or pigment biosynthesis, seed formation, and starch metabolism.

30. (Amended)

The method of claim 2, wherein the maize Ds element is further defined as containing overlapping sequences having homologous regions, which sequences, when homologously combined, results in a functional gene.

33. (Amended)

The method of claim 30, wherein the gene is selected from the group consisting of: genes useful for disease resistance; genes useful for male sterility; genes useful for environmental condition tolerance; and genes useful for [the commercially-enhancing a biosynthetic pathway] fruit ripening, oil or pigment biosynthesis, seed formation, and starch metabolism.

35. (Amended)

The recombination construct of claim 18, wherein the gene is selected from the group consisting of: genes useful for disease resistance; genes useful for male sterility; genes useful for environmental condition tolerance; and genes useful [for the commercially-enhancing a biosynthetic pathway] fruit ripening, oil or pigment biosynthesis, seed formation, and starch metabolism.